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Determination of a ligand binding site in a protein: a fluctuation of a protein obtained from brownian dynamics simulation reveals a ligand binding site

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What are the differences between the ligand-binding site and other cavities on a protein? We took notice of hydrophobicity of the site and developed a method to find the binding site in a protein using the empirical hydrophobic potential. We tested our method on many protein-ligand complexes whose 3-D structures are experimentally known, and it was shown that our method can successfully find the binding sites in 92% of the test sets. However, the most hydrophobic site was not always the binding site when more than one hydrophobic sites were detected. So, we pay attention to the flexibility of the site. For 4 proteins on which plural hydrophobic sites are detected, we applied brownian dynamics simulations to calculate the fluctuations of the sites. As a result, the most flexible site was the binding site. It is indicated that the flexibility of the binding site might be common feature of a protein. Therefore, a combination of hydrophobicity and flexibility is very useful for determination of the ligand-binding site to construct the protein-ligand complex.